Using uncertainty quantification to constrain dynamic neuron modeling parameters

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Abstract

The goal of this work is to develop computational and statistical tools to enable uncertainty quantification of neural simulations. We extend fourier-based techniques to use experimental data in the refinement of neuron simulations parameters and topology.

Computer simulations of neural activity are valid constructs within a restricted operating regime. This work calculates limits or bounds within which one can be confident that a simulation is dynamically behaving in the same manor as an experiment. To that end we have implemented common neurological ion-channel models (e.g. Hodgkin-Huxley, Connor-Stevens) in a dynamic cable-equation format within a circuit simulator, Xyce (xyce.sandia.gov); see simulation outline below. This allows one to use a netlist style syntax to describe a collection of neurons for simulation. As with any circuit simulation, the model parameters for the circuit components are critical in determining the circuit's performance.

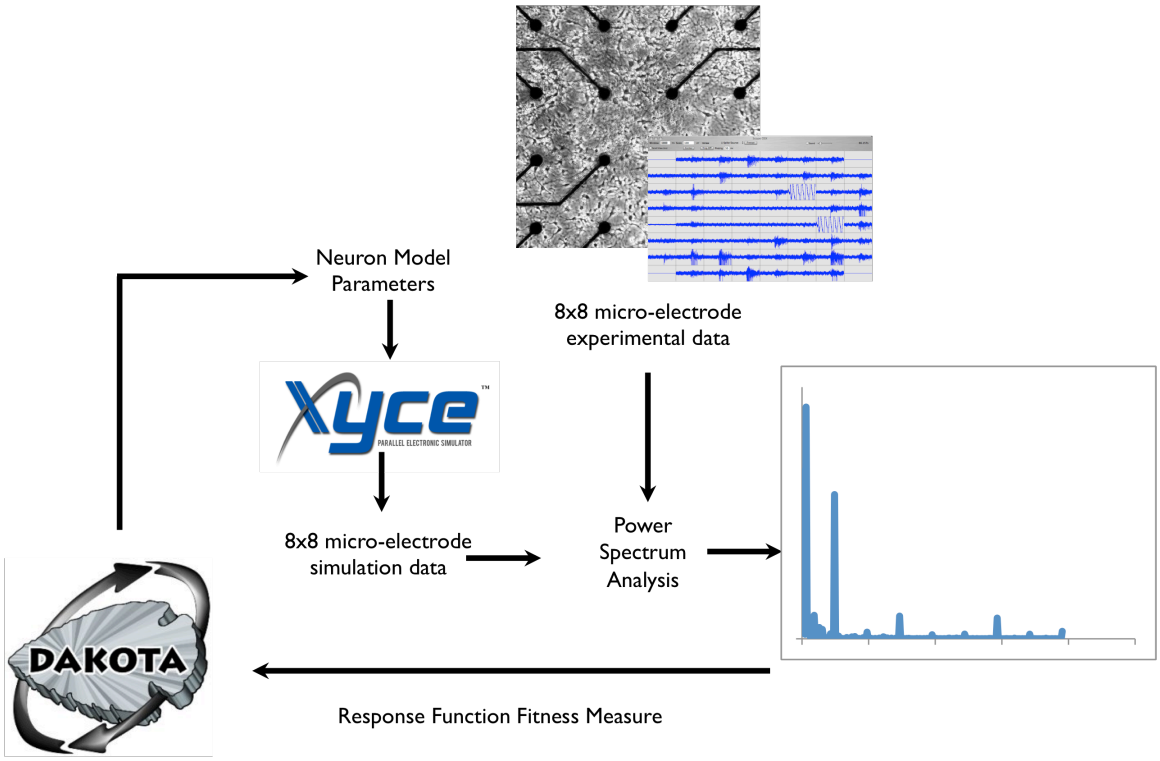
Experimental data from micro-electrode array recordings on hippocampus cell cultures (data courtesy of B. Wheeler & D. Khatami, U. of Florida) were used to bound the simulation parameters. Specifically, transient data from the simulations is compared to micro-electrode array data. However, direct comparison cannot be made between the experimental and simulation data in the transient domain because of the unknown initial condition state of the experiments and the unknown topology of the experimental system. Two approaches are taken to mitigate these problems. First, by transferring the results to a frequency domain and constructing a power-spectra, one can compare the two sets of data and infer important properties. Differences between the simulated and experimental power-spectra allow one to both optimize the fit of the simulation to the experiments and calculate the uncertainty allowed in the simulation's model parameters. Second, since the underlying cellular topology is unknown for the experimental system, random topologies (and some directed topologies for verification) are generated and used in the simulation. Thus, both the model parameter space is searched and the circuit topology space is searched for systems that dynamically mimic the experiments.

This allows one to quantify what is unknown or unrepresented in both the experiments and simulations leading to a better understanding of both results. As

expected, low-fidelity data can be matched with a low fidelity, or simple model. When the experimental system becomes more complex (i.e. exhibits long term potentiation) more complex models are needed to fully describe the data.

Finally, because the computational process can be automated, tens to thousands of simulation parameters and or topologies can be tested for their sensitivity on the results. To confront the geometric scaling for simulation needs, we utilize a hierarchial parallel simulator. Xyce can run on multiple processors in a distributed or shared memory system and the uncertainty quantification controller, Dakota, can control and dispatch multiple jobs in parallel. Thus, one can efficiently utilize a computing cluster where each compute node has multiple cores and there are multiple compute nodes.

We will present results comparing simulated and experimental systems under both un-stimulated and post-stimulation conditions. Uncertainty quantification for the Hodgkin-Huxley and more complex Connor-Stevens neuron models indicates that sodium and potassium ion conductance terms are critical for this experimental system. We will include bounds within which the simulations are relevant and discussion of scalability to larger systems.



Simulation and Uncertainty Quantification Loop: Experimental system and typical transient data show at top. Sample power spectra shown on lower right

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